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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/697,497
Filing Date: October 30, 2003
Appellant(s): SUFFIN ET AL.

Thomas C. Howerton
For Appellant

EXAMINER'S ANSWER

This is in response to a supplemental appeal on April 22, 2009 appealing from the Office action mailed August 7, 2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

2002/0147196 A1 QUESSY ETAL. 10-2002

Zakrzewska et al. Oxcarbazepine: A New Drug In the Management of Intractle Trigeminal Neuralgia". J. Neurol Neurosurg Psychiatry, 52(4):472-6 (1989).

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quessy et al. (US 2002/0147196 A1) of record further in view of Zakrzewska et al. (#84, PTO-1449), (Journal of Neurology, Neurosurgery, and Psychiatry 1989) of record.

Quessy et al. teach a pharmaceutical composition comprising **bupropion** and sodium channel blockers including **oxcarbazepine and lamotrigine** useful for the treatment of **neuropathic pain**. (page 5, claims 1-3). Quessy et al. illustrate the composition comprising **bupropion and lamotrigine** (page 5, Example 3, claim 6). Quessy et al. teach that using the test compound lamotrigine in a pre-clinical experiment, no adverse side effects were observed. ([0038]). Quessy et al. also teach that the composition can be formulated with **mixtures of NE-reuptake inhibitors which exert analgesic activity (analgesics)**. (page 1, [0009], [0010]). Quessy et al. further teach that the composition can be formulated as a **transdermal patch**, **sterile injectable solution**, **tablet**, **capsules**, **oral liquid** or **a sterile liquid for injection** and can be formulated with suitable **polymeric** materials. ([0021]-[0027]). Quessy et al. additionally teach that the composition manifests **synergism** in the treatment of neuropathic pain ([0009]). Quessy et al. lastly teach that there is a need for a pharmaceutical composition that can alleviate neuropathic pain or/its symptoms effectively. (page 1, [0004], [0007]).

However, Quessy et al.'s illustrated composition (example 3) uses lamotrigine with bupropion, rather than oxcarbazepine as instantly claimed.

Zakrzewska et al. teach that **oxcarbazepine** possesses **antineuralgic properties,** is effective in the management of intractable **trigeminal neuralgia,** and elicits an **excellent** therapeutic response in **controlling pain without side effects**. (abstract).

It would have been obvious to one of ordinary skill in the art to modify the composition of Quessy et al. by replacing lamotrigine with oxcarbazepine, because Quessy et al. teach that bupropion can be formulated with any one of disclosed sodium channel blockers including oxcarbazepine or lamotrigine, and because Quessy et al. teach that oxcarbazepine and lamotrigine are equivalents both having the anti-neuralgic properties for treating neuropathic pain in combination with bupropion. Further, Zakrzewska et al. also teach that oxcarbazepine has no side effects. One of ordinary skill in the art would be motivated to make such a modification with oxcarbazepine in order to fulfill the need of a pharmaceutical composition and providing variety for the treatment of neuropathic pain, not only possessing anti-neuralgic properties but also lacking side-effects as taught by Zakrzewska et al. There is a reasonable expectation of successfully treating neuropathic pain without side effects with a combination of bupropion and oxcarbazepine, the latter well taught by Zakrzewska et al. as possessing excellent anti-neuralgic properties with an excellent therapeutic response in controlling pain. With regard to further combining with a third drug as set forth in claim 2 and the specified formulation as set forth in claim 3, all deemed obvious because Quessy et al.

teach that NE-reuptake inhibitors exert analgesic activity (analgesics) and, therefore, can be incorporated in the obvious combination and because the various formulations set forth in claim 3 are taught by Quessy et al. as suitable formulations for the obvious combination. One would have been motivated to further incorporate analgesics in a mixture to the combination in various formulations disclosed by Quessy et al. in order to successfully formulate an ultimate regimen for the treatment of neuropathic pain possessing at least one synergistic effect disclosed by Quessy et al. without a side effect. Absent any evidence to contrary, there would have been a reasonable expectation of successfully improving the anti-neuropathic pain composition of Quessy et al. by combining bupropion and oxcarbazepine in order to fulfill the need of a pharmaceutical composition that can alleviate neuropathic pain without as a side effect.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

(10) Response to Argument

Appellants arguments have been fully considered but they are not persuasive. Appellants argue that Quessy et al. does not provide any teaching that oxcarbazepine and lamotrigine have equivalent efficacies and the Examiner has improperly argue that lamotrigine and oxcarbazepine have the same analgesic activity and efficacy of treating neuropathic pain. This is not found to be persuasive because the instant invention of a formulation comprising oxcarbazepine and an antidepressant, wherein said

antidepressant is bupropion, is fully taught and suggested by Quessy et al. (see Quessy et al. claims 1, 2 and 3). Quessy et al. clearly named the species of norepinephrine reuptake inhibitor as bupropion and the species of a sodium channel blocker as oxcarbazepine can be formulated as a pharmaceutical composition because of their therapeutic effect of treatment of neuropathic pain. (see Quessy et al. claims 14, 15 and 16 as well as claims 1, 2 and 3). Further, Zakrzewska et al. teaches the advantages of oxcarbazepine having excellent therapeutic response in controlling pain without side effects in a patient suffering from trigeminal neuralgia (neuropathic pain). One of ordinary skill in the art would be motivated to interchange oxcarbazepine with lamotrigine in Quessy et al's formulation in order to achieve the expected benefit of oxcarbazepine having excellent therapeutic response in controlling pain without side effects.

Appellants argue that the Examiner has not fulfilled the burden of showing that oxcarbazepine is equivalent to lamotrigine. This is not found to be persuasive because the Quessy et al. reference fully teaches that both oxcarbazepine and lamotrigine can be employed as a sodium channel blocker for the treatment of neuropathic pain. Therefore, this reference clearly teaches that either one of them can be combined with bupropion in a single formulation for the treatment of neuropathic pain. Appellants assert that oxcarbazepine and lamotrigine share a common mechanism of action. However, Appellants argue that they are not structurally similar and therefore, there is a significant difference between lamotrigine and oxcarbazepine, and it would not be expect that they have the same therapeutic efficacy. This is not found persuasive

because the issue is not whether the compounds lamotrigine and oxcarbazepine have different unrelated chemical structure. The issue is whether there is a clear teaching and suggestion from the prior art, Quessy et al., that sodium channel blockers such as lamotrigine and oxcarbazepine can be formulated with bupropion as a pharmaceutical composition because they have a therapeutic benefit in the treatment of neuropathic pain. Appellants argue that Zakrzewska's observation that oxcarbazepine has no apparent side effect does not provide a proper motivation for a combination with Quessy et al. because it was overlooked that Quessy et al. teach that lamotrigine also has no side effects. This is not found persuasive because the Examiner has provided the Zakrzewska reference to show the similar benefits of oxcarbazepine in treatment of neuropathic pain next to Quessy et al's illustrated example of employment of lamotrigine in the combination with bupropion. That Quessy et al. selected lamotrigine with bupropion in their formulation rather than oxcarbazepine as their example as a sodium channel blocker do not suggest that oxcarbazepine does not work in their bupropion formulation, but rather that lamotrigine is better suited their need. There remains, even after Quessy et al.'s disclosure, a reasonable expectation of success that oxcarbazepine would work in a pharmaceutical composition with bupropion, given that oxcarbazepine and lamotrigine are interchangeable as sodium channel blockers.

Appellants argue that Appellants have provided two Declarations (XII Evidence Appendix, Attachments 3 & 4) in past Office Actions to demonstrate that lamotrigine and oxcarbazepine have opposite neurophysiologic effects (i.e., the effects of oxcarbazepine is not predictable based upon the effects of lamotrigine), therefore, they

are not interchangeable. Appellants argue that in the Declarations have shown that oxcarbazepine presents unexpected results. The Declarations have been reviewed and fully considered by the Examiner. However, they are not persuasive because again, the issue is not whether the two sodium channel blockers are different in their chemical/physical characteristics, the real issue is whether the clear teaching and suggestion from Quessy et al. that these two compound have the same therapeutic effect in the treatment of neuropathic pain and they can be combined with bupropion in a single pharmaceutical composition. As far as a formulation for the treatment of neuropathic pain comprising a combination of bupropion and a sodium channel blocker, oxcarbazepine is interchangeable with lamotrigine because it is fully suggested and clearly taught by Quessy et al. Appellants' apostrophe showing of whether these two agents have different neurophysiologic effects due to their unrelated structural differences does not change the most relevant teaching of Quessy et al. that these two compounds have the same therapeutic effect in the treatment of neuropathic pain and they can be combined with bupropion in a single pharmaceutical composition.

Appellants argue that both of the references (Attachments 1 & 2) teach that neuropathic pain can, and does involve the central nervous system and the Appellants provided relevant data showing that the central nervous system effects of oxcarbazepine (either alone or in combination with bupropion are unexpected (i.e., for example, opposite) that of lamotrigine, either alone or in combination with bupropion. because again, the issue is not whether the compounds lamotrigine and oxcarbazepine have different unrelated chemical structure. The issue is whether there is a clear

teaching and suggestion from the prior art, Quessy et al., that sodium channel blockers such as lamotrigine and oxcarbazepine can be formulated with bupropion as a pharmaceutical composition because they have the same therapeutic benefit in the treatment of neuropathic pain. As far as a formulation for the treatment of neuropathic pain in a combination comprising bupropion and a sodium channel blocker, oxcarbazepine is interchangeable with lamotrigine because it is fully suggested and clearly taught by Quessy et al. that those two compounds have the same therapeutic effect in the treatment of neuropathic pain and, therefore, can be combined with bupropion in a single pharmaceutical composition.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.
Respectfully submitted,

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